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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/614,283	07/08/2003	Tsu-An Hsu	8842.0002	2562

22852 7590 04/10/2006

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EXAMINER	
GARVEY, TARA L	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 04/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/614,283	HSU ET AL.	
	Examiner	Art Unit	
	Tara L. Garvey	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,11-14,19,21-26 and 33-41* is/are pending in the application.

4a) Of the above claim(s) *19,25 and 33-41* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5, 11-14, 21-24 and 26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-5,11-14,19, 21-26 and 33-41 are pending. Receipt is acknowledged of an amendment filed on December 20, 2005.

Response to Arguments

Priority

Receipt is acknowledged of an amendment to the specification filed on October 30, 2003 claiming priority to provisional application 60/394,269.

Claim Objections

The objection of claim 30 is withdrawn in view of applicant's cancellation of the claim.

Claim Rejections - 35 USC § 112

The rejection of claims 1-18, 21-24, 26-30 and 32 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in view of applicant's amendment.

Claim Rejections - 35 USC § 102

The rejection of claims 1-5, 11 and 13 under 35 U.S.C. 102(b) as being anticipated by Urabe et al (Gene (1997) volume 200, pages 157-162) is withdrawn in view of applicant's amendment.

The rejection of claims 1, 3-5, 11 and 13 under 35 U.S.C. 102(e) as being anticipated by van Zonneveld et al (US 6,447,768) is withdrawn in view of applicant's amendment.

The rejection of claims 1, 3-5, 11 and 13 under 35 U.S.C. 102(e) as being anticipated by Whitley et al et al (US 6,764,675) is withdrawn in view of applicant's amendment.

The rejection of claims 1-5, 11 and 13 under 35 U.S.C. 102(b) as being anticipated by Agarwal et al (US 6,194,212) is withdrawn in view of applicant's amendment.

The rejection of claims 1, 3-5, 11 and 14 under 35 U.S.C. 102(b) as being anticipated by Seguela et al (US 2003/0219858) is withdrawn in view of applicant's amendment.

The rejection of claims 1, 2, 4, 5, 11, 12, 21, 22, 24 and 26 under 35 U.S.C. 102(b) as being anticipated by Finkelstein et al (Journal of Biotechnology (1999) volume 75, pages 33-44 referenced in the IDS submitted on September 27, 2004) is withdrawn in view of applicant's amendment.

Claim Rejections - 35 USC § 103

The rejection of claims 1-5, 11 and 13 under 35 U.S.C. 103(a) as being unpatentable over Urabe et al (Gene (1997) volume 200, pages 157-162) in view of Kirkegaard et al (US 2004/0052765 A1) is withdrawn in view of applicant's amendment.

The rejection of claims 1-5, 11-13, 21- 24 and 26 under 35 U.S.C. 103(a) as being unpatentable over Finkelstein et al (Journal of Biotechnology (1999) volume 75, pages 33-44 referenced in the IDS submitted on September 27, 2004) in view of Urabe et al (Gene (1997) volume 200, pages 157-162) is withdrawn in view of applicant's amendment.

New Grounds of Rejection

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-5, 11-13, 21, 22, 24 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Finkelstein et al (Journal of Biotechnology (1999) volume 75, pages 33-44 referenced in the IDS submitted on September 27, 2004) in view of McMinn, P (FEMS Microbiology Reviews (2002) volume 26, pages 91-107).

Claims 1-5, 11-13, 21- 24 and 26 are drawn to a biological vector or a baculovirus transfer vector that expresses at least two cistrons and comprises a promoter operably linked to the nucleotide sequence for the two cistrons and an EV71 IRES nucleotide sequence linked to at least one downstream cistron, where the EV71 IRES sequence provides IRES activity.

Finkelstein et al teaches a bicistronic baculovirus vector that comprises the baculovirus polyhedrin promoter (Ppol) and an EMCV IRES separating two reporter genes such as chloramphenicol transferase (CAT) and firefly luciferase (LUC) and recombinant baculoviruses (abstract, page 34, right column, first full paragraph, page 35, left column, last paragraph bridging right column, page page 36, Figure 1 and page 37, Figure 2 and right column, last paragraph bridging page 38, left column). The vector would inherently have IRES activity since the EMCV IRES is known to have IRES activity. The EMCV IRES contained within the baculovirus vector and recombinant baculovirus is capable of having IRES activity in a mammalian cell (page 38, left column, first full paragraph, lines 28-30 and right column, lines 13-16). Furthermore, Finkelstein et al teach the baculovirus vector and the recombinant baculovirus contained in host cells such as different species of insect cells and demonstrate that the EMCV IRES has

residual IRES activity in these cells (page 43, left column, first full paragraph, lines 20-25).

Finkelstein et al does not teach using the EV71 IRES in the dicistronic baculovirus vector or recombinant baculovirus.

McMinn, P teaches that enterovirus 5' UTR contain an internal ribosome entry site (IRES), which regulates enterovirus replication through control of cap-independent translation of the polyprotein. Furthermore, McMinn teaches the existence of EV71 IRES cDNA that is able to replace and function in a chimeric virus for the PV1(M) IRES (page 102, left column, first full paragraph).

It would have been obvious to one of ordinary skill in the art to modify the teachings of Finkelstein et al to use an IRES from EV71 in the baculovirus vector. One would have been motivated to do so in order to receive the expected benefit, as suggested by McMinn, of obtaining more efficient expression of two cistrons separated by an EV71 IRES in a baculovirus vector system. Absent of any evidence to the contrary, there would have been reasonable expectation in using an EV71 IRES because others have successfully used an IRES in dicistronic viral vectors.

Claims 1-5, 11-13, 21- 24 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Finkelstein et al (Journal of Biotechnology (1999) volume 75, pages 33-44 referenced in the IDS submitted on September 27, 2004) and McMinn, P (FEMS Microbiology Reviews (2002) volume 26, pages 91-

107) in further view of Urabe et al (Gene (1997) volume 200, pages 157-162; made of record in the office action mailed September 22, 2005).

Finkelstein et al and McMinn et al have been described previously.

Finkelstein et al and McMinn et al do not teach that one of the cistrons comprises a therapeutic gene.

Urabe et al teaches using either an HCV IRES or EMCV IRES in a dicistronic AAV vector that contains a therapeutic gene (abstract, page 158, left column last paragraph, Figure 1 and right column bridging page 159, left column, page 159, right column, first full paragraph bridging page 160, left column, line 1, page 160, right column, second and third full paragraphs, page 161, left column, first paragraph and right column, first full paragraph).

It would have been obvious to one of ordinary skill in the art to modify the combined teachings of Finkelstein et al and McMinn, P to express a therapeutic gene in the baculovirus vector. One would have been motivated to do so in order to receive the expected benefit, as suggested by Urabe et al, of using the viral vector for treatment of disease. Absent of any evidence to the contrary, there would have been reasonable expectation in using a dicistronic viral vector for potential treatment of a disorder.

Claims 1-5, 11 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Urabe et al (Gene (1997) volume 200, pages 157-162; made of record in the office action mailed September 22, 2005) in view of McMinn, P (FEMS Microbiology Reviews (2002) volume 26, pages 91-107).

Claims 1-5, 11 and 13 are drawn to a nucleic acid vector and a biological vector that comprise a promoter operably linked to at least two cistrons which can be either a reporter gene or a therapeutic gene and a nucleotide sequence for EV71 IRES that is operably linked to at least one of the downstream cistrons and to host cells containing the vectors.

Urabe et al teaches a dicistronic adeno-associated vector (AAV) that comprises a CMV promoter, either a reporter gene such as luciferase or a therapeutic gene, the HCV-IRES or EMCV-IRES and a selectable marker gene and mammalian 293 cells that contain the constructs (abstract, page 158, left column last paragraph, Figure 1 and right column bridging page 159, left column, page 159, right column, first full paragraph bridging page 160, left column, line 1, page 160, right column, second and third full paragraphs, page 161, left column, first paragraph and right column, first full paragraph).

Urabe et al does not teach using an EV71 IRES in a dicistronic adeno-associated viral vector.

McMinn, P teaches that enterovirus 5' UTR contain an internal ribosome entry site (IRES), which regulates enterovirus replication through control of cap-independent translation of the polyprotein. Furthermore, McMinn teaches the existence of EV71 IRES cDNA that is able to replace and function in a chimeric virus for the PV1(M) IRES (page 102, left column, first full paragraph).

It would have been obvious to one of ordinary skill in the art to modify the teachings of Urabe et al to use an IRES from EV71 in the AAV vector. One would have been motivated to do so in order to receive the expected benefit, as

suggested by McMinn, of obtaining efficient expression of two cistrons separated by an EV71 IRES in a AAV vector system. Absent of any evidence to the contrary, there would have been reasonable expectation in using in using an EV71 IRES because others have successfully used an IRES in dicistronic viral vectors.

Claims 1, 3-5, 11 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over van Zonneveld et al (US 6,447,768; made of record in the office action mailed September 22, 2005) in view of McMinn, P (FEMS Microbiology Reviews (2002) volume 26, pages 91-107).

Claims 1, 3-5, 11 and 13 have been described previously.

van Zonneveld et al teaches a dicistronic adenoviral vector that comprises a CMV promoter, NO synthase cDNA, IRES from EMCV and VEGF 121 or FGF4 cDNA as the angiogenic factors and cells containing the adenoviral vector (abstract, column 5, lines 40-67 bridging column 6, lines 1-34 and column 18, lines 15-57).

van Zonneveld et al does not teach using an EV71 IRES in a dicistronic adenoviral vector.

McMinn, P teaches that enterovirus 5' UTR contain an internal ribosome entry site (IRES), which regulates enterovirus replication through control of cap-independent translation of the polyprotein. Furthermore, McMinn teaches the existence of EV71 IRES cDNA that is able to replace and function in a chimeric virus for the PV1(M) IRES (page 102, left column, first full paragraph).

It would have been obvious to one of ordinary skill in the art to modify the teachings of van Zonneveld et al to use an IRES from EV71 in the AAV vector. One would have been motivated to do so in order to receive the expected benefit, as suggested by McMinn, of obtaining efficient expression of two cistrons separated by an EV71 IRES in an adenoviral vector. Absent of any evidence to the contrary, there would have been reasonable expectation in using in using an EV71 IRES because others have successfully used an IRES in dicistronic viral vectors.

Claims 1, 3-5, 11 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over by Whitley et al et al (US 6,764,675; made of record in the office action mailed September 22, 2005) in view of McMinn, P (FEMS Microbiology Reviews (2002) volume 26, pages 91-107).

Claims 1, 3-5, 11 and 13 have been described previously.

Whitely et al teaches a dicistronic herpes simplex virus (HSV) vector that comprises an Egr-1 promoter, the p40 and p35 subunits of mIL-12 separated by an IRES from EMCV and mammalian cells containing the vector (abstract, column 5, lines 10-21, column 6, lines 40-67 bridging column 7, lines 1-59 and column 8, lines 48-67 bridging column 9, lines 1-31).

Whitely et al does not teach using an EV71 IRES in a dicistronic HSV vector.

McMinn, P teaches that enterovirus 5' UTR contain an internal ribosome entry site (IRES), which regulates enterovirus replication through control of cap-

independent translation of the polyprotein. Furthermore, McMinn teaches the existence of EV71 IRES cDNA that is able to replace and function in a chimeric virus for the PV1(M) IRES (page 102, left column, first full paragraph).

It would have been obvious to one of ordinary skill in the art to modify the teachings of Whitely et al to use an IRES from EV71 in the HSV vector. One would have been motivated to do so in order to receive the expected benefit, as suggested by McMinn, of obtaining efficient expression of two cistrons separated by an EV71 IRES in an HSV vector. Absent of any evidence to the contrary, there would have been reasonable expectation in using in using an EV71 IRES because others have successfully used an IRES in dicistronic viral vectors.

Claims 1-5, 11 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Agarwal et al (US 6,194,212; made of record in the office action mailed September 22, 2005) in view of McMinn, P (FEMS Microbiology Reviews (2002) volume 26, pages 91-107).

Claims 1-5, 11 and 13 have been described previously.

Agarwal et al teaches a dicistronic retroviral vector comprising a retroviral promoter such as LTR and an IRES from EMCV separating the RevM10 gene and the marker gene Lyt-2 and cells containing the retroviral vector (column 2, lines 62-67 bridging column 3, lines 14-43, column 4, lines 7-23 and column 7, lines 34-67 bridging column 8 lines 1-53).

Agarwal et al does not teach using an EV71 IRES in a dicistronic retroviral vector.

McMinn, P teaches that enterovirus 5' UTR contain an internal ribosome entry site (IRES), which regulates enterovirus replication through control of cap-independent translation of the polyprotein. Furthermore, McMinn teaches the existence of EV71 IRES cDNA that is able to replace and function in a chimeric virus for the PV1(M) IRES (page 102, left column, first full paragraph).

It would have been obvious to one of ordinary skill in the art to modify the teachings of Agarwal et al to use an IRES from EV71 in the retroviral vector. One would have been motivated to do so in order to receive the expected benefit, as suggested by McMinn, of obtaining efficient expression of two cistrons separated by an EV71 IRES in a retroviral vector. Absent of any evidence to the contrary, there would have been reasonable expectation in using in using an EV71 IRES because others have successfully used an IRES in dicistronic viral vectors.

Claims 1, 3-5, 11 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Seguela et al (US 2003/0219858; made of record in the office action mailed September 22, 2005) in view of McMinn, P (FEMS Microbiology Reviews (2002) volume 26, pages 91-107).

Claims 1, 3 and 11 have been described previously. Claim 14 limits the vector to being contained in a bacterial cell.

Seguela et al teaches a bicistronic nucleic acid vector that comprises a CMV promoter and two nucleic acid sequences encoding ASIC2A and ASIC3

polypeptides separated by an IRES from EMCV and E. coli cells containing the vector (page 18, right column, paragraph [0186]).

Seguela et al does not teach using an EV71 IRES in a bicistronic nucleic acid vector.

McMinn, P teaches that enterovirus 5' UTR contain an internal ribosome entry site (IRES), which regulates enterovirus replication through control of cap-independent translation of the polyprotein. Furthermore, McMinn teaches the existence of EV71 IRES cDNA that is able to replace and function in a chimeric virus for the PV1(M) IRES (page 102, left column, first full paragraph).

It would have been obvious to one of ordinary skill in the art to modify the teachings of Seguela et al to use an IRES from EV71 in the retroviral vector. One would have been motivated to do so in order to receive the expected benefit, as suggested by McMinn, of obtaining efficient expression of two cistrons separated by an EV71 IRES in a nucleic acid vector. Absent of any evidence to the contrary, there would have been reasonable expectation in using in using an EV71 IRES because others have successfully used an IRES in bicistronic nucleic acid vectors.

Claims 1-5, 11 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kirkegaard et al (US 2004/0052765 A1; made of record in the office action mailed September 22, 2005) in view of McMinn, P (FEMS Microbiology Reviews (2002) volume 26, pages 91-107).

Claims 1-5, 11 and 13 have been described previously.

Kirkegaard et al teaches a dicistronic vaccinia virus vector that comprises a promoter operable linked to the exogenous nucleic acid sequence and a poliovirus IRES separating coding sequence for poliovirus 3A and GFP. The poliovirus 3A protein is used to elicit or enhance an immune response, which reds on a therapeutic gene (page 5, paragraphs 0049, 0054 and 0055 and page 9, left column, paragraph 0009).

Kirkegaard et al does not teach using an EV71 IRES as the biological vector.

McMinn, P teaches that enterovirus 5' UTR contain an internal ribosome entry site (IRES), which regulates enterovirus replication through control of cap-independent translation of the polyprotein. Furthermore, McMinn teaches the existence of EV71 IRES cDNA that is able to replace and function in a chimeric virus for the PV1(M) IRES (i.e. poliovirus) (page 102, left column, first full paragraph).

It would have been obvious to one of ordinary skill in the art to modify the teachings of Kirkegaard et al to use a poxvirus as the biological vector for expression of two cistrons. One would have been motivated to do so in order to receive the expected benefit, as suggested by McMinn, P, of obtaining efficient expression of two cistrons in a vaccinia virus construct. Absent of any evidence to the contrary, there would have been reasonable expectation in using an EV71 IRES to express two cistrons since viral IRES sequences are commonly used in vectors for this purpose and the poliovirus IRES and EV71 IRES appear to be interchangeable.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tara L Garvey whose telephone number is (571) 272-2917. The examiner can normally be reached on Monday through Friday 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) (http://pair-direct.uspto.gov) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7

business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

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Tara L Garvey, Ph.D.
Examiner
Art Unit 1636

TLG

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